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The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision, unless so designated by other documentation.

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13. ABSTRACT (Maximum 200 words)

The focus of our project during the reporting period was on the feasibility analysis of using the cognoscope for functional imaging of the brain. The Cognoscope was designed based on the concept of using near-infrared spectroscopy (NIRS). NIRS allows for resolution of cortical activity non-invasively. By using magnetoencephalography (MEG) our effort was focused on the verification of the Cognoscope. After receiving IRB approvals, we began our tests on the human subject brain functions imaging by means of both the Cognoscope and the MEG. Five subjects have been tested and MEG data has been analyzed and compared to the Cognoscope images. The results are promising in terms of detecting brain images that correspond to different muscle movements that human subjects performed, as described in our IRB protocol. In order to pursue this study further, we have determined that the resolution of the Cognoscope must be improved in terms of both sensor density and scan rate. In the process of increasing the resolution of the Cognoscope we intend to also eliminate the need for human subjects to not have any hair over the areas of the head where the cognoscope is placed.

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Development of Advanced Active haptic System for Musculokelelton Exoskeleton Interactions

Defense Advanced Research Projects Agency
Submitted to:
Dr. John Main (DARPA)
Dr. David Stepp (ARO)

Final Report
August 31, 2005

Grant Number: DAAD190310312

Principal Investigator: Dr. Rahmat A. Shoureshi
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DARPA Final Report

1 Project Objectives:

Our first and second year objectives were to identify, develop, and possibly modify a means of noninvasive brain imaging. Once a device was found, a protocol for clinical testing needed to be defined. A means of verifying the output was decided and the submission process to an Internal Review Board began. The review process has ended successfully and the next phase of work has begun. The protocol recommended a feasibility study to examine the utility of using near infrared spectroscopy (NIRS) of the brain to predict distinct motor movements. NIRS proved to be a useful means of motor control prediction but the current device that we have been using has been determined to be insufficient for our end goals.

The group found a device, the Cognoscope, to perform the brain imaging. The Cognoscope provides light sources and detectors on a band worn around the head. Consisting of four LED sources and ten Opto 101 photodiode detectors, this multi-channel device claims to be able to make an entire sampling pass in 200 ms, but in testing appears to only sample three times per second. The LEDs provide two different wavelengths of Near-Infrared light, which easily passes through biological tissues and is highly scattered. The penetration depth is roughly 7cm depending upon the person's skull thickness. This available depth allows for visualization of the cerebral cortex. Literature reviews have shown that different groups have used this Near-IR technique for a number of varying studies including prefrontal cortex research that looks at thought processes, monitoring of the visual cortex during stimulation and even some very basic monitoring of the motor cortex during simple finger movements.

The research of our group will be the first major step toward tracking brain activation and patterns associated with specific activations of large motor movements. The Progress to Date section and the appendix will provide specific information about how we are proceeding with clinical trials and what the clinical trials entail.

2 First Year Research:

Our protocol was submitted to the University of Denver's Internal Review Board and was originally approved pending two modest changes (approval available in Appendix A). Before submission of the protocol, consent forms, patient questionnaires, and protocol application, each of the researchers directly involved in the human trials successfully completed a Human Subjects Training class and passed the mandatory exam (patient forms of consent and information release available in Appendices B and C).

The final form of the protocol outlines the procedure for working with human subjects from their screening visit (to assure acceptance into the trial) to the measurements collected and how these measurements will be collected (the complete protocol is available in Appendix D). To summarize the protocol briefly, we intend to use

20 healthy volunteers between the ages of 18 – 30. Each of these volunteers will have three separate testing visits and one initial screening visit. The screening visit is simply to verify their good health, attain written informed consent, and be certain that each volunteer knows and is comfortable performing the necessary tasks. Each of the testing visits is identical. During each of these visits, the person will have to wear the Cognoscope over the motor cortex and surface electromyography (SEMG) electrodes at target muscle locations. Data will be collected continuously and simultaneously from both the Cognoscope and SEMG electrodes for the duration of each task. The SEMG is proposed to serve as a validation tool so that we can directly correlate in situ, specific muscle activation to brain activation patterns developed simultaneously. The tasks involve single and double arm movements, gripping, single and double arm lifting, normal walking, stair walking, and stepping over objects.

3 Second Year Research:

In accordance with the recommendation from the internal review board, we have run preliminary tests to verify that the cognoscope is an adequate device for meeting our projects goals. Through our collaboration with the University of Colorado Health Sciences Center, Department of Psychiatry, Biomagnetic Imaging Center, we have run tests on four subjects and collected magnetoencephalogram (MEG) (figure 1 left) and near-infrared spectroscopy (NIRS) (figure 1 right) data for a variety of muscle motions and somatosensory stimuli. We have determined that the cognoscope's NIRS readings do reflect the MEG activations that occur during single muscle group activation and somatosensory stimulation. Areas of MEG activity closely match previously documented motor cortex region mapping leading us to believe that the MEG comparisons are a useful validation tool. The NIRS indicates that an increase in blood volume and a decrease in blood oxygenation occur in the same areas that activate in the MEG data.

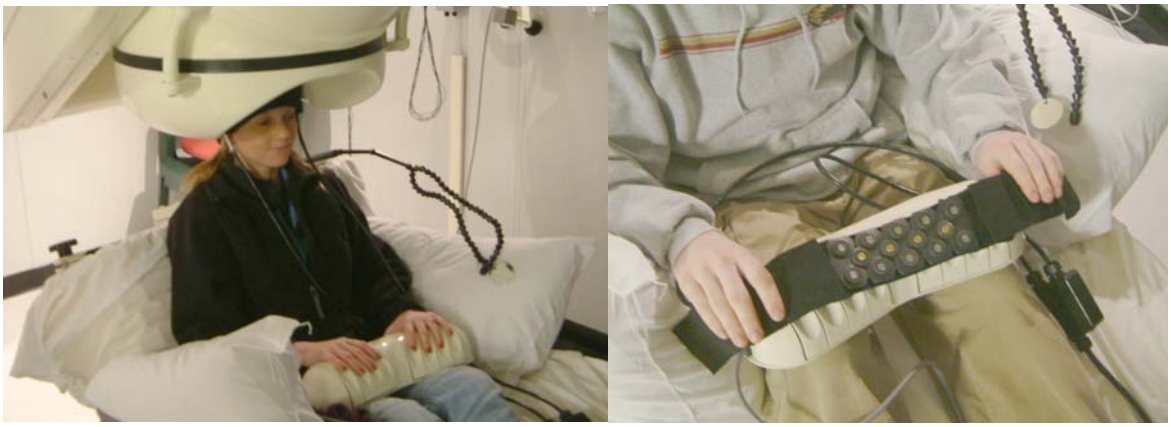

Figure 1: Left: MEG and NIRS data recording setup. Right: Cognoscope with sensors facing up.

Although the NIRS does have a good correlation with the MEG data, the resolution of the cognoscope is not high enough to prevent the possibility of confusion between muscle groups that are close to one another within the motor cortex (figure 2). The current scan rate for the cognoscope may also lead to inadequate response time for

active control of a robotic limb. A higher performance array of sensors focused on a single area of interest within the motor cortex is the most likely solution for overcoming these obstacles. A faster scan rate like that of the MEG would produce more responsive movement from a robotic limb (figure 3).

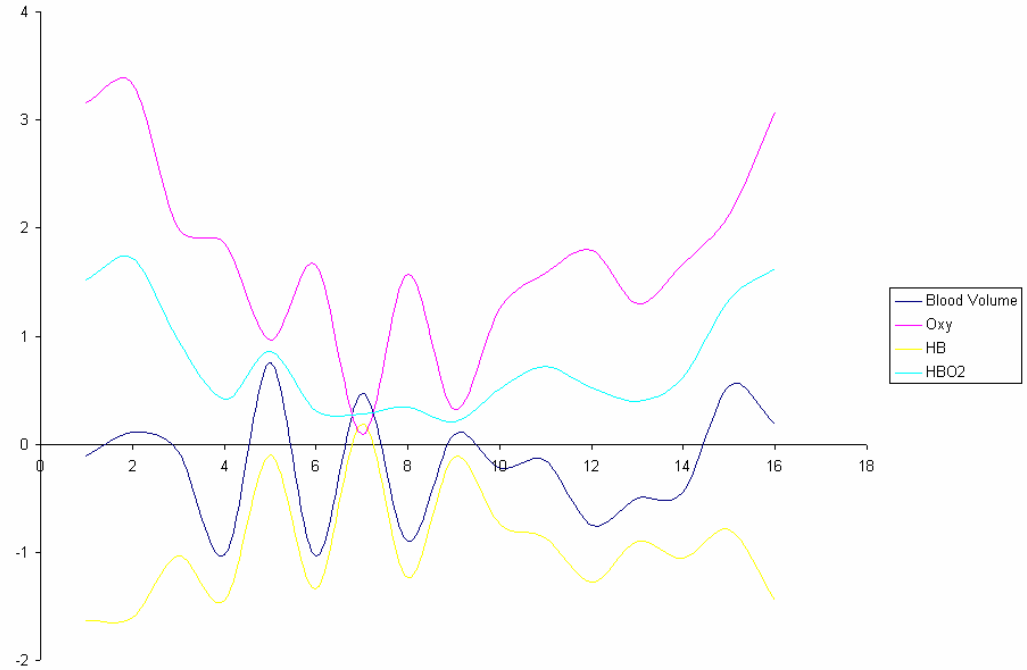

Figure 2: NIRS data for entire activation averaged by channel. Indicates area of activation to be strongest around channel 7. (Note: odd number channels are front row, even are back row.)

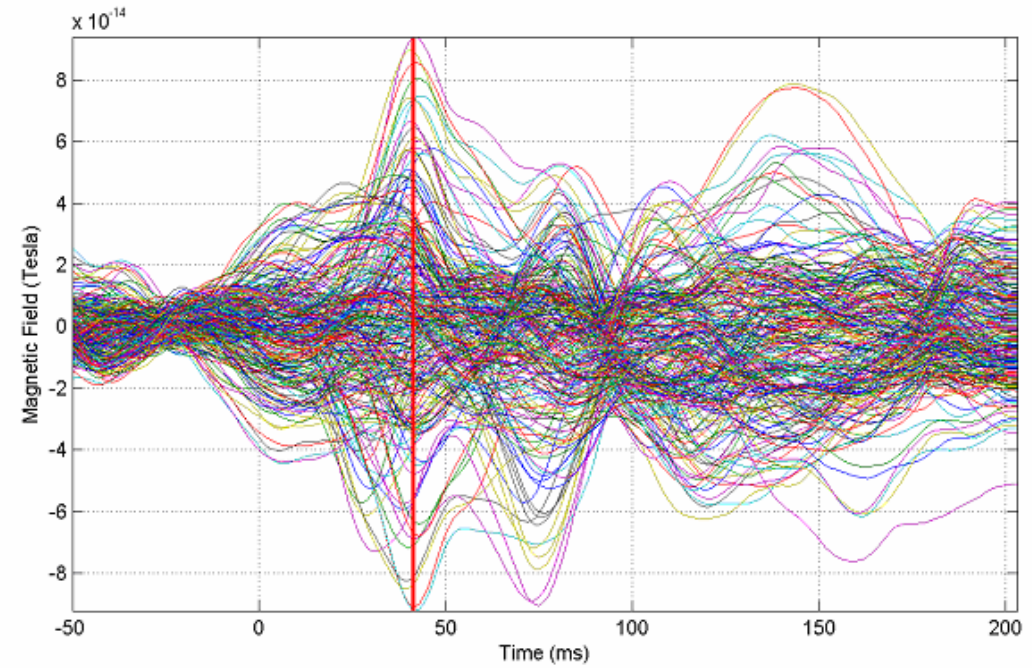

Figure 3: Graph of MEG data displayed as signal vs. time identifying the time of activation with a vertical red line.

4 Continuation of Research:

4.1 New NIRS Device:

Our first objective is to create a new NIRS device that is capable of a higher resolution in the area(s) that we intend to monitor. This device should have at least 20 channels over an area of several square inches and be able to make complete scans of this area in under 200 ms. The new device will also work without requiring the user to shave their head in order to get accurate readings. This goal will be accomplished through the use of a plastic optic in order to avoid scattering from hair between the transmitter and the scalp.

4.2 Additional Data Collection and Analysis:

Once our new NIRS device has demonstrated that the desired readings can be obtained, clinical trials will commence. We are currently seeking 20 total participants. Each participant will be tested a total of three times (falling on three separate days). The main goal of data analysis is to correlate data from the EMG sensors to the patterns in brain activity, and generate appropriate proactive triggers to the exoskeleton. The latter function will be fully researched once a clear correlation can be established between events generated by the muscles and patterns in the brain.

Two sets of data are generated – by the EMG sensors attached to various muscle groups and by the thought sensing device that is recording brain activity. EMG sensors are measuring voltages using sixteen different sensors at a rate of 20 samples per second or 20 Hertz. This is approximately a Megabyte of data every hour. Data thus generated is routinely logged to a database for archival purposes and to create a complete audit trail for offline analysis. No sensitive information is stored inside the database. The data is suitable to be exported to different team members without compromising the subject's privacy. Every new subject receives a unique ID that is used by the system to follow the subject.

One of the main difficulties in processing signals from EMG sensors is the noise that is associated. Generally, various filters or algorithms based on Independent Component Analysis are applied to refine the signal and suppress spurious artifacts. Correlation would be computed by either using one of the standard statistical packages such as MATLAB or by developing more refined methods based on modified nearest-neighbor algorithms.

In addition, the data capturing hardware would be integrated with a visualization subsystem. This would be an interactive, realtime correlation establishment and visualization software. It would also give the user the ability to tune different parameters for best performance. This visualization software would be built using graphical user interfaces and lets the user focus on the signals that are being recorded. The user interface would offer two display modes: a normal view-mode and a quality view-mode. The quality view-mode displays the consecutive signals superimposed. This way it is easy to see if the signals change from one electrode to the other. Furthermore, in a

separate window, the cross-correlation values would be displayed for all superimposed signals. Checking the acquired signals during the acquisition is crucial for good signal quality.

4.3 Further Research Using NIRS:

In addition to the above-mentioned tasks, in the future we would like to submit protocols for two more clinical trials to be approved by our IRB. One would focus on expanding the collaborations with the Psychology group at UCHSC. More in-depth studies of MEG versus Near-IR imaging to provide more conclusive evidence for very specific brain activation patterns associated with muscle movement. Possibly even to focus on optimal source-detector placement. There is some inherent delay in the NIRS system; if this could be offset by LED sources placed over the pre-motor cortex, then the response time could be greatly improved.

The second protocol we would like to gain approval on involves the work of Dr. Steven Ojemann, our Neurologist. Dr. Ojemann's work uses implantable electrodes place on the brains of subjects that have come in for surgery to monitor brain activity.

4.4 Conclusion:

As a result of the feasibility study, it has been determined that near-infrared spectroscopy should be able to be used to sense motor cortex activity. Analysis of magnetoencephalogram and near-infrared spectroscopy data recorded during the same muscle activation indicate that regions of the motor cortex that correspond to muscle groups being activated are accurately reflected in both sets of data. However the accuracy of the cognoscope that we are currently using is inadequate for real-time control of a mechanical limb.

In order to continue our research on motor cortex monitoring in order to control a robotic limb, we must first develop a device more suited to our purposes to prevent negative results in future phases of this project. For this reason the time that this project will take to complete has been extended by at least one year and has required the expertise of additional faculty at the University of Denver.

Appendix:

Appendix A: Internal Review Board Approval

Appendix B: Patient Consent Form Example

Appendix C: Patient Release of Medical Information for Research Example

Appendix D: Protocol for Near-Infrared Feasibility Study

Appendix A: Internal Review Board Approval

UNIVERSITY OF
DENVER

Office of Sponsored Programs
2199 S. University Blvd.
Denver, CO 80208
303.871.2121
Fax 303.871.2623

December 4, 2003

Rahmat Shoureshi
Department of Engineering & Computer Science
University of Denver
Denver, CO 80208

Subject: Human Subject Review
TITLE: "Feasibility Study for Motor Cortex Tracking with Near-IR Brain Imaging."
IRB: 03127
PURPOSE: Sponsored Agreement
SPONSOR: Defense Advanced Research Projects Agency (DARPA)
NEW APPLICATION

Dear Dr. Shoureshi:

The Institutional Review Board for the Protection of Human Subjects has reviewed the above named project. The project has been approved for the procedures and subjects described in the protocol at the **November 11, 2003** meeting. This approval is effective for twelve months. We will be sending you a continuation application for this project in **August 2004.** This form must be completed and returned to the Office of Sponsored Programs if the project is to be continued. If you do not receive this application, please contact Dawn Nowak, Office of Sponsored Programs, 303-871-4052.

Attached is a copy of your consent form, a brief summary of your responsibilities regarding the use of human subjects, and a copy of the University of Denver Assurance of Compliance with Health and Human Services Regulations for Protection of Human Subjects.

The Institutional Review Board appreciates your cooperation in protecting subjects and ensuring that each subject gives a meaningful consent to participate in research projects. If you have any questions regarding your obligations under the Assurance, please do not hesitate to call Dawn Nowak.

Sincerely yours,

Dr. Maria Riva / DN

Dr. Maria Riva
Chair, Institutional Review Board
for the Protection of Human Subjects

Attachments

Appendix B: Patient Consent Form Example

INFORMED CONSENT FOR A STUDY EXECUTED AT THE UNIVERSITY OF DENVER

Feasibility Study for Motor Cortex Tracking with Near-IR Brain Imaging

Principal Investigator: Rahmat Shoureshi

SUBJECT CONSENT FORM

Project Description/Purpose

You are being asked to take part in a research study to determine feasibility of using Near-IR brain imaging to track motor movements. You must sign a consent form before participating. If you are interested in being part of this study, you will be asked to answer some questions regarding your health status and you will be asked to undergo a brief physical examination. You will also be asked to fill out a brief questionnaire. This project is being supervised by Rahmat Shoureshi, University of Denver, Denver CO, 80208, (303)871-3787.

You have been asked to participate because you are a healthy subject between the ages of 18 and 30 and you either maintain a shaved head or you are willing to shave your head to be involved in the study.

This study involves the use of a device known as a Cognoscope. The Cognoscope has two parts: light sources that are near the infrared spectrum and light detectors. The other device to be used is a magnetoencephalography system (MEG). The Cognoscope device may allow researchers to determine when a specific muscle contraction is about to take place just before it happens. The purpose of this study is to evaluate the feasibility of the Cognoscope to identify specific brain imaging patterns that are related to these muscle contractions.

You may not participate in any part of this study before you have given your consent. The consent form is designed to protect the study volunteers so please read through it carefully if you are interested in participating in this study. The study will attempt to complete data collection on 20 patients total (this includes both locally and nationally).

Procedures

If you agree to take part in this study: you will receive additional screening and test visits as detailed in the remainder of this section. If you agree to participate in this study, you will be asked to answer some brief health history questions to ensure that you are a good study candidate. As a study volunteer you will be asked to wear, on a trial basis, the Cognoscope headpiece and asked to sit in the MEG device. You will be asked to wear the Cognoscope and undergo MEG testing for a short period of time [75 – 120 minutes] and under supervision on more than one occasion [3 times]. The study will be completed by November of 2004.

SCREENING

The study will be explained and written informed consent obtained from you prior to the initiation of any procedures. There will be a pre-visit screening to determine your interest and acceptance into the study. If you are interested in being part of this study, you will be asked to answer some questions regarding your health status and you will be asked to undergo a brief physical examination. At this time you also will be asked to fill out a short medical questionnaire. If it is determined that you are not an appropriate candidate after your questionnaire has been completed, you will be disqualified from the study. You will be asked to describe your medical history as completely and accurately as possible. The history will record your age; sex; all of your medical conditions and all the medications you take. You will have a basic physical exam. You will be screened to ensure that you meet the inclusion and exclusion criteria. Screening procedures may be divided into more than one visit, if deemed necessary.

SUBSEQUENT VISITS

After the screening visit, you will be asked to return for testing periods on three different occasions. ALL TESTING VISITS WILL TAKE PLACE AT THE UNIVERSITY OF COLORADO HEALTH SCIENCES CENTER IN THE NEUROIMAGING DEPARTMENT. At each of these visits, you will be asked to undergo testing while MEG data is collected and you will be also asked to wear the Cognoscope headpiece for data collection. There will be one task that you will need to complete during each visit. The first task will take place on your first visit. While you are seated, you will grasp an object with your right and then your left hand, lifting the objects up off a table, and then returning them to the table. You will be asked to repeat this a number of times during the data collection. The objects you will be lifting will weigh roughly 1 pound. The data collection will first take place from the MEG system and then the exact same procedure will take place with the Cognoscope sensor.

The second visit will involve taking measurements while you perform single arm movements. You will be repeatedly moving your arm away from or toward you body. These movements will be repeated several times. Again, you will first perform the movement while MEG data is collected and then again while the Cognoscope collects data.

The third visit will focus on leg movements. You will again be seated. You will be asked to extend your legs, one at a time, and then return your leg to the rest position. Again this movement will be made repeatedly and once the MEG data is collected, it will be done again with the Cognoscope sensor.

The visits will be separated by no less than 2 days and no more than 15 days. If you agree to participate in this study, you will need to make special visits to the Neuroimaging center at the University of Colorado Health Sciences Center.

On completion of the study, you will discontinue use of the Cognoscope and MEG hardware. You may not keep any instruments used by you.

Potential Risks of Participant
At present there are no known risks involved with wearing the Cognoscope sensors or undergoing MEG data collection. The study may include risks that are not known at this time.

Benefits
This study is designed for the researcher to learn more about whether brain images recorded from the Cognoscope can truly predict and be correlated to muscle activity. This study is not designed to treat any illness or to improve your health.

Sponsor
This study is funded by Defense Advanced Research Projects Agency DARPA through the US Army Research Office.

Cost to Subject
There is no cost to you for participating in this study.

Subject Payment
You will receive $100.00 compensation for your time and travel needs. This is intended to help with the travel costs associated with being part of this research study and the time commitment of the research. This compensation will be paid to you in the form of a check and sent to your permanent residence through the U.S. mail. Should you not be able to complete the study through the third visit, the time/travel reimbursement will be prorated at $33.33 for each completed study visit.

Study Withdrawal and Voluntary Participation
Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you do not take part in this study you will not be penalized for your decision. You will not lose any benefits or medical care to which you are entitled.

If you chose to take part, you have the right to stop at any time. If there are any new findings during the study that may affect whether you want to continue to take part, you will be told about them.

The study doctor may decide to stop your participation without your permission if he or she thinks that being in the study may cause you harm, or for any other reason. Also the sponsor may stop the study at any time.

Invitation for Questions
You will receive a copy of this consent form. Please ask questions about this research or consent either now or in the future. You may direct your questions to Rahmat Shoureshi at (303)871-3787. If you have questions regarding your rights as a research subject, please contact Dr. Maria Riva, Chair, Institutional Review Board for the Protection of Human Subjects, at (303) 871-2484, or Dawn Nowak, Office of Sponsored Programs at (303) 871-4052, or write to either at the University of Denver, Office of Sponsored Programs, 2199 S. University Blvd., Denver, CO 80208. You may also contact the study sponsor, Dr. David M. Stepp, at (919)549-4329 in the US Army Research Office**.**

Confidentiality

Dr. Shoureshi and the above mentioned sponsors will treat your identity with professional standards of confidentiality. However, information from this study will be submitted to the sponsor and if appropriate to the U.S. Food and Drug Administration. The consent form signed by you may be inspected and/or copied by:

- The sponsor
- An agent for the sponsor

And may be inspected and or copied by:

- The FDA
- Department of Health and Human Services (DHHS) agencies
- Governmental agencies in other countries which have authority to regulate the study

Because of the need to release information to these parties, absolute confidentiality cannot be guaranteed. The results of this research study may be presented at meetings or in publications; however, your identity will not be disclosed in those presentations.

I understand that there are exceptions to the promise of confidentiality. If information is revealed concerning suicide, homicide or child abuse and neglect, it is required by law that this be reported to the proper authorities. In addition, should any information contained in the study be the subject of a court order or lawful subpoena, the University of Denver might not be able to avoid compliance with the order or subpoena.

New Information

Any important information about the study device that becomes available during the course of this study, which may influence your decision to continue in the study, will be made known to you. The doctors conducting this study will answer any questions you may have about the study devices, exams or tests.

All information and test results that could be used to identify you will be kept strictly confidential. This means that no one will be able to see the information collected in this study except the medical staff at the doctor's office and some representatives from the University of Denver. Your name will not appear in any publications, public discussions or presentations. Information collected from your medical record and this study may be added to a computerized data collection system using codes instead of names. Confidentiality will be ensured by the use of one computer that will contain all the patient data and is password protected. All hard copies of information will be kept in locked file cabinets.

Compensation for Injury

If you have questions about injury related to the research, you may call Dr. Shoureshi and/or your private physician. Dr. Shoureshi should be informed about any injury you experience while you take part in this study. The university will not provide any monetary compensation in the event of an injury to a subject; however, if you are hurt by this research, we will provide medical care with no cost to you.

Authorization

I have read this paper about the study or it was read to me. I understand the possible risks and benefits of this study. I know that being in this study is voluntary. I choose to be in this study: I know I can stop being in this study and my withdrawal will not penalize me in any way. I will get a copy of this consent form.

Signature: _____ Date: _____

Subjects parent or guardian [print name]: _____

Consent form explained by: _____ Date: _____

Signature _____ Investigator: _____ Date: _____

Appendix C: Patient Release of Medical Information for Research Example

Authorization To Use or Release Health Information About Me For Research Purposes *Authorization: Enrollment into Research*	Study Title: Feasibility study for motor cortex tracking with Near-IR brain imaging DU IRB Protocol #:

I _____ *(Subject's Full Name)* **authorize**

Rahmat Shoureshi, PhD *(PI or Physician Name)* **and staff members of**

University of Denver *(Facility Name)* **working for him/her to use the following health information about me for research:** *(Please check the appropriate boxes. NOTE: If a category is checked "yes" and a line follows the category, you MUST describe type and number of the procedures done.)*

No Yes

☐ ☒ Name and/or phone number
☐ ☒ Demographic information (age, sex, ethnicity, address, etc.)
☐ ☒ Diagnosis(es)
☐ ☒ History and/or Physical
☒ ☐ Laboratory or Tissue Studies: _____
☒ ☐ Radiology Studies: _____
☒ ☐ Testing for or Infection with Human Immunodeficiency Virus (HIV) (or results) **
☒ ☐ Procedure results: _____
☒ ☐ Psychological tests: _____
☐ ☒ Survey/Questionnaire: brief health questionnaire
☒ ☐ Research Visit records
☐ ☒ Portions of previous Medical Records that are relevant to this study
☒ ☐ Billing or financial information
☒ ☐ Drug Abuse **
☒ ☐ Alcoholism or Alcohol abuse **
☒ ☐ Sickle Cell Anemia **
☒ ☐ Other (Specify): _____

***** ***when this category of information is included for VA patients, an authorization expiration date or condition is required on page 3***

For the Specific Purpose of

☒ Collecting data for this research project
☐ Other* _____

**Cannot say "for any and all research", "for any purpose", etc.*

If my health information that identifies me is also going to be given out to others outside the facility, the recipients are described on the next page(s).

☐ *No personally identifiable health information about me will be disclosed to others*

The PI (or staff acting on behalf of the PI) will also make the following health information about me available to: (check all that apply and **describe type and number of the procedures** done where applicable)

Recipient _Paul Rullkoetter, the Study Coordinator_

No Yes

☒ ☐ All Research Data Collected in this Study (if you check this box Yes, no other boxes need to be checked in this section)

☐ ☒ Name and phone number
☐ ☒ Demographic information (age, sex, ethnicity, address, etc.)
☐ ☒ Diagnosis(es)
☐ ☒ History and Physical
☒ ☐ Laboratory or Tissue Studies: _____
☒ ☐ Radiology Studies: _____
☒ ☐ Testing for or Infection with Human Immunodeficiency Virus (HIV) (or results) **
☒ ☐ Procedure results: _____
☒ ☐ Psychological tests: _____
☐ ☒ Questionnaire/Survey: _brief health questionnaire_____
☒ ☐ Research Visit records
☒ ☐ Portions of previous Medical Records that are relevant to this study
☒ ☐ Billing/Charges
☒ ☐ Drug Abuse **
☒ ☐ Alcoholism or Alcohol **
☒ ☐ Sickle Cell Anemia **
☒ ☐ Other (Specify): _____

***when this category of information is included for VA patients, an authorization expiration date or condition is required on page 3*

For the Specific Purpose of

☒ Evaluation of this research project
☐ Evaluation of laboratory/tissue samples
☒ Data management
☒ Data analysis
☐ Other*: _____

**Cannot say "for any and all research", "for any purpose", etc.*

For additional Recipients, copy this page as needed.

I give my authorization knowing that:

- I do not have to sign this authorization. But if I do not sign it the researcher has the right to not let me be in the research study.
- I can cancel this authorization any time.
  - I have to cancel it in writing.
  - If I cancel it, the researchers and the people the information was given to will still be able to use it because I had given them my permission, but they won't get any more information about me.
  - If I cancel my authorization, I may no longer be able to be in the study.
  - I can read the Notice of Privacy Practices at the facility where the research is being conducted to find out how to cancel my authorization.
- The records given out to other people may be given out by them and might no longer be protected.

I will be given a copy of this form after I have signed and dated it.

This authorization will expire on**:** _____ (Date) OR

☒ The end of the research study

☐ Will not expire

☐ _____

(Describe dates or circumstances under which the authorization will expire. This is required for VA patients, when using or disclosing information on AIDS/HIV testing or results, sickle cell anemia, and treatment for drug or alcohol abuse, and alcoholism.)

ADDITIONAL INFORMATION: This research study if for the benefit of creating a device to be used by an exoskeleton for actuation of the exoskeleton movement. The important results from this study will be the SEMG and Cognoscope data collected and this data will be saved and used in such a way as to be completely confidential. Another important result from this study will be the determination of any correlations that exist between surface electromyographic data and blood flow data (found by the Cognoscope). None of this data will be personally identifiable.

_____

_____

_____

Subject's Signature Date

_____

Signature of Legal Representative (If applicable) Date

_____

Name of Legal Representative (please print)

_____

Description of Legal Authority to Act on Behalf of Patient

Appendix D: Protocol for Near-Infrared Feasibility Study

Protocol Version 1

Feasibility Study for Motor Cortex Tracking with Near-IR Brain Imaging

Introduction

The purpose of this protocol is to determine the feasibility of implementing diffuse optical tomography (DOT), specifically near infrared (near IR), for the prediction of motor function. We are hoping to determine the feasibility of using near IR for predicting specific motor movements such as grasping, walking, and stepping over objects. This project is funded through the Defense Advanced Research Projects Agency (DARPA) and is being performed by a research team of faculty in the School of Engineering and Computer Science, with some graduate student support. This is one of many institutions in the country working on an Exoskeleton project with Department of Defense (DOD) funding.

This protocol proposes a feasibility study to examine the utility of using near infrared spectroscopy (NIRS) of the brain to predict distinct motor movements. If NIRS proves to be a useful means of motor control prediction, then the NIRS would provide an excellent means of actuation for Exoskeleton movement. All parts of this protocol are non-invasive and we are proposing testing of only healthy subjects.

Background

Motion Tracking

Of all the human activities, the walking gait has probably been modeled and studied by more researchers than any other activity. In the computer vision community, researchers have built kinematic models of the human body in order to determine a sequence of poses of the body in video succession [1-3]. These models are not very useful in our application, however, since they do not model or predict motions. Other computer vision researchers have developed models for activities (primarily walking, but also for gesture and facial expression recognition) based on temporally localized features extracted with Principle Component Analysis (PCA) [4], neural nets [5], activity templates [6-10], and hidden Markov models (HMMs) [11-20].

Biomechanics researchers have also modeled human activities, but again seem to have focused on gait, most frequently on walking gaits. One approach, the “Top-Down Analysis of Gait” refined by Vaughan et al. in [21], divides the human gait generation system into seven serial components that describe the physiologic sequence of events that occurs from initiation of a central nervous system impulse to generation of sufficient ground reaction forces at the foot/floor interface to propel the body forward. Whereas this approach could theoretically model much of the complexity of the gait process (including variations due to obstacles or terrain), the higher level processes are incompletely understood and can, in practice, not be easily modeled. Another model of gait uses a decomposition of the gait “task” into sub-tasks, for instance (1) support of

the body against collapse during weight acceptance, (2) balance during single limb support, and (3) safe and coordinated limb advancement during swing [22, 23]. With further decomposition and with a formulation of the sub-(sub-)tasks as competing behaviors it may be possible to generate a predictive model, but as currently defined the model is not predictive. A recent paper by Prentice et al. [24] describes a simple neural net for predicting the muscle activity required for walking. A similar approach might be applied to this project, but whether such a model can adapt to changes in the gait pattern is unclear. An approach described in [25] examines modeling of stepping over obstacles and might be a successful approach to extending models to variations due to terrain variations or obstacles. These last two approaches do predict specific motions, and appear to be the most applicable to our problem. Incorporating muscle actuation inputs into the models should be a natural extension of this study.

Therefore, by having human subjects performing typical motions that a soldier would experience, we will be able to assess musculoskeletal dynamics, muscle activation and prediction of joint forces and torques.

Neurophysiological Sensors

In 1925, Liddell and Sherrington introduced an idea that the basic unit of voluntary and reflex movement consisted of a motor nerve and the muscle fibers innervated by that nerve [26]. This concept of the motor unit has since become central in the modern understanding of nerve and muscle physiology. With the advent of the cathode ray oscilloscope and concentric needle electrode in the 1920's, the technique of needle electromyography (EMG) became a clinically useful tool for studying motor unit electrical potentials in the diagnosis of nerve and muscles disorders [27].

The technique of surface electromyography (SEMG), however, has received relatively little attention in the general literature of electrodiagnostic medicine. The explanation lies in its poor resolution of the microphysiologic features of motor unit morphology and innervation patterns. But unlike conventional invasive monopolar or concentric needle electrodes that record from a limited surrounding area, surface electrodes are capable of recording from larger areas of muscle without causing significant discomfort. When properly rectified and integrated, SEMG activity correlates with the force generated by a muscle [28]. In recent years, this feature of SEMG as well as its non-invasiveness have made it increasingly useful as an objective tool to evaluate subjective measures of muscle fatigue and discomfort [29].

The ability of SEMG amplitude to estimate muscle activity in a reproducible and accurate manner remains limited by many technical factors. These include low signal to noise ratio, high inter and intra-subject variability, and cross talk, a term describing the detection of signals from more than one muscle through a pair of electrodes. In dynamic muscle testing, SEMG signals are further obscured by movement and geometrical artifacts [30]. These issues and others limit the current ability of SEMG to evaluate muscle activity during changes in task.

Surface EMG technology continues to evolve and is driven in part by the burgeoning field of ergonomic studies. Different research groups have developed different methods for acquiring SEMG data and addressing technical problems [31]. As yet, there is no

clear consensus regarding the best techniques, in part because techniques vary depending on the parameters to be measured. Information on normalization procedures and actual normative data also are scant. In the area of neck muscle activity during light work and semi-static tasks, some effort has been made to achieve a consensus regarding technical procedures [32]. However, the current state of the field requires redefinition of procedures based on generally recognized electrical and physiological principles for each new clinical problem or question to be addressed. The broader refinement and resolution of these issues over time will make the wider application of this technology possible.

Dr. Miguel Nicoleleis at Duke University has pioneered the use of neural implants to study the brain. He and only about a half-dozen teams around the world are pursuing the same goals: gaining a better understanding of how the mind works and then using that knowledge to build implant systems that would make brain control of computers and other machines possible. Such systems are called “hybrid brain-machine interfaces”, or HBMIs. Similar activities are being carried out at the Laboratory for Human and Machine Haptics at MIT.

In the long run, Nicolelis predicts that HBMIs will allow human brains to control artificial devices designed to restore lost sensory and motor functions. Paralysis sufferers, for example, might gain control over a motorized wheelchair or a prosthetic arm – perhaps even regain control over their own limbs.

Ongoing experiments in other labs are showing that this idea is credible. At Emory University, neurologist Philip Kennedy has helped severely paralyzed people communicate via a brain implant that allows them to move a cursor on a computer screen (see “Mind Over Muscles.” TR March/April 2000 [33]). And implants may also shed light on some of the brain’s unresolved mysteries. Nicolelis and other neuroscientists still know relatively little about how the electrical and chemical signals emitted by the brain’s millions of neurons let us perceive color and smell a few tenths of a second before it actually happens.

Tracking of Motion and Motor Cortex

In order to make the exoskeleton follow the movements of the soldier, there needs to be a transducer system that can measure or predict the soldier’s motions.

Measurement of accelerations and loads

One way that the soldier’s motions could be tracked would be via measurement of limb accelerations using accelerometers. Such a transducer would be useful for measuring the onset of motion (i.e. from a static posture) but would be subject to errors once the soldier is moving.

Another method of measuring movement would be via load transducers between the exoskeleton and the soldier’s body. Any delay in the response of the exoskeleton will cause a force to be developed between the soldier and the exoskeleton due to the inertia of the exoskeleton. While this type of transducer system will have some utility, it is desirable to minimize any loads between the soldier and the exoskeleton.

Measurement of muscle activity and contraction

Since there will be a delay inherent in any control system, it would be preferable to predict motion before it actually occurs. In order for the limbs to move voluntarily, muscle contraction needs to occur. There are several physiologic changes to muscle that occur immediately preceding force production.

The most common way of measuring the onset of muscle contraction is via Electromyography (EMG). EMG is a way of monitoring the electrical activity of muscle and can be correlated with force production. Two techniques exist for measuring EMG signals; surface vs. indwelling electrodes. The nature of indwelling electrodes, that they need to be inserted through the skin and into the muscle, makes them impractical for this application. Surface electrodes would be much more appropriate but have several limitations. One limitation is that they are not very selective, they can pick up the activity of neighboring muscles. This limitation can be overcome via use of an electrode array with sophisticated signal processing algorithms. Another limitation is that consistent measurement requires constant electrical properties between the electrode and the skin. In a normal circumstances the electrical properties of the skin change with activity leading to changes in the apparent EMG signal. However, in spite of some possible challenges to face with SEMG measurements, this will be our chosen form of EMG monitoring. The use of surface EMG monitoring is very well established and there is no reason to believe that our use of SEMG will cause any unnecessary risk to volunteers.

Measurement of neural activity

The time interval between muscle contraction and force production is on the order of 50 to 500 ms. While this delay might provide enough time to compensate for time lag in the control system, it would be ideal if this interval between intention and motion could be increased. The only way to do this would be to measure the neural activity that causes muscle contraction.

Voluntarily muscle contraction is planned and executed in the motor cortex of the brain. Activity in this brain region is increased during planning and execution of motor activities. Various techniques can be used for measuring neural activity in the motor cortex. Until recently, most of these techniques required large, non-wearable, equipment.

Diffuse optical tomography (DOT) is an emerging medical imaging modality in which tissue is illuminated by near-infrared light from an array of sources, the multiply scattered light which emerges is observed with an array of detectors, and then a model of the propagation physics is used to infer the localized optical properties of the illuminated tissue. The three primary absorbers at these wavelengths are water, oxygenated and deoxygenated hemoglobin. All have relatively weak absorption. This fortuitous fact provides a spectral window through which we can attempt to localize absorption primarily by the two forms of hemoglobin and scattering in the tissue. The most important current applications of DOT are detecting tumors in the breast and imaging the brain [34, 35]. The greater blood supply of tumors compared to surrounding

tissue provides a target absorption inhomogeneity to image. A similar idea allows us to image bleeding in the brain, while the same association between cerebral activity and increased oxygen supply which underlies functional magnetic resonance imaging (fMRI) also allows functional imaging with DOT. The modality has seen a tremendous upsurge in interest over the last ten years but still presents a number of significant technological and signal processing challenges.

The interest in DOT has been motivated by several factors, including:

- The ability of near infrared (NIR) light to penetrate relatively deeply (several centimeters) into tissue without causing harm to the tissue.
- The sensitivity of infrared (IR) light to the physiologically important concentration of oxygen-carrying components of blood.
- The low relative cost of the equipment for this type of imaging, compared to CT or MRI.

Given the recent developments in Spring 2002 by the National Space Biomedical Research Institute (NSBRI) [36] and the developing field of Near IR brain imaging [37, 38], imaging brain functions is feasible and our effort will be focused on pattern recognition/classification of blood flow in the brain indicative of specific motor movements.

The application of fNIR for brain imaging emerged in the early 1990s. It is a harmless, non-invasive means of brain imaging that is carried out more easily than magnetic resonance imaging (MRI) since a person does not have to lay completely still for long periods of time. The primary use of fNIR has been for psychological and emotional studies of brain function and little if any effort has been spent tracking patterns for motor movement. One common use of it has been for lie detector tests [39]. Obviously numerous studies have been done using fNIR for brain imaging and each of these studies has used an assortment of people from a group of women in their 70's to babies, to high school students and so on [37, 38, 40].

Objectives

The objectives of this study are to monitor a small group of individuals for the purpose of feasibility testing of the near IR process to determine motor movement. The study is completely non-invasive by using only physical sensors that will be applied on the surface of the skin. The sensors that will be employed are already commonly used in the medical field. A Cognoscope will be our means of functional near-IR brain imaging by means of light emitting diodes. The light sources that are to be placed on the surface of the skin and directly over the forebrain are LEDs or light emitting diodes. LEDs are commonly used for a number of other purposes in everyday life – lights in our homes and offices, lanterns, headlamps, etc. As an analogy, the proposed research is really no different than holding a flashlight to your head – except there are detectors to pick up the light that is reflected.

Methods

Recruiting Methods

The patients that will be participating in the proposed study will be drawn from the population of healthy patients available at the University of Denver. In the event that there are not enough volunteers at the University of Denver, poster advertisements will be used to try and find additional volunteers at the Air Force Academy. The most immediate future user of this developing product will be soldiers enlisted in one of the branches of the U.S. Military, therefore, ideal patients will be 18 to 30 years in age and in excellent physical condition and mental health. We intend to recruit patients by means of posters that will be placed at each of the mentioned locations. The posters will solicit interested persons between the ages of 18 and 30, who feel they are in good physical condition, to contact the Study Coordinator for more information.

Consent Procedures

The person obtaining consent will have received the proper training under the guidelines of the University of Denver's Internal Review Board. All researchers directly involved in the clinical study will have received the required training. The setting in which the consent will be obtained is at the University of Denver under the guidance of Rahmat Shoureshi, the P.I., after ascertaining interest in participating. Any patient who wishes to be a part of the study will be presented with the consent form. If they have any questions about the form or the procedure, they can ask the researcher working with them. They may then either accept or decline. All volunteers will be assured that their participation is completely voluntary and that no reprimands will befall them if they are not interested in participating. Each interested subject will be asked to describe the procedure in their own words to assess the subject's comprehension of the study and what their participation will involve. The consent forms will be filed in a patient folder along with other documentation that needs to accompany that particular individual. The patient folders will be kept in a locked file cabinet and treated as confidential information. Any person not involved in the study will not have access to any patient information. Any patient that agrees to be involved in the study will not have access to any other participant's information.

Treatment, Intervention, or Observation

Testing will take place at the University of Denver. A few simple motor functions will be analyzed for this particular protocol. These tasks will include: grasping (both with the right and left hands individually and then simultaneously, using a light object and then a heavy object), walking normally for a few steps, walking up and down steps, and stepping over an object.

For each task, an array of anywhere from three to six near IR sources and an array of several reflected light detectors will be placed on the subject's forehead. Data collection will occur at a rate of 3 Hz for the Cognoscope. In addition to the IR light sources and receiving sensors, SEMG data will be collected at the specific muscle activation locations on the subject. The SEMG data will serve as a control to what is observed from near IR readings.

The grasping task.

The subject will be seated at a table with both feet on the floor and sitting straight. Each subject's hands will be placed on the table in front of them, palms down and resting as though preparing to type on a keyboard. A full, unopened 12oz soda can will be placed near each hand. When the subject is told to begin, they will grasp and lift up the can closest to their right hand and then return it to the table and place their hand back in the resting position. When they are given the signal again, they will then reach for the can closest to their left hand and repeat the procedure. On the third and fourth readings, the subject will select which can they are going to pick up and follow the same procedure. When these four trials are done, the soda cans will be replaced with 5 pound weights and the same procedure just described will be carried out – right then left and then two of their own choosing (right or left hand).

When the data recording for individual hand grasping has been completed a text book will replace the two items on the table and when the subject is given the signal, they will reach with both hands to grasp the text book, lift it up off the table and then replace it to the starting position and place their hands back in the resting position. This will be repeated once more. After two trials with the book, a ten-pound weight will replace the book and two trials will commence with this object.

For this task, surface electromyographic sensors will be placed on the dorsal and ventral aspect of each forearm. Data collection from SEMG will take place at a rate of at least 20 Hz and will occur simultaneously with collection from the near IR Cognoscope.

Walking normally.

For this task the subject will be standing behind a piece of colored tape on the floor. Three feet in front of them will be another piece of colored tape. The subject will be told when to begin walking, will walk to the second piece of tape and then stop. This will be repeated twice. During walking, the SEMG adhesive electrodes will be placed on the dorsal and ventral aspects of each upper leg segment (ie. one on each quadriceps and one on each hamstring), the dorsal aspect of the lower leg in the calf area and the ventral aspect of the lower leg just lateral to the tibia.

Stairs – up and down.

A set of box stairs, such as used in a gait lab, will be used for this task. The subject will begin by standing facing the steps. When they are told, they will walk up the steps and then stop. They will then turn around and wait for the queue to walk down the steps and then stop. The up and down sequence will be repeated one more time. For the stair task, the same electrodes will be used as in walking, but 4 additional electrodes will be added. These will be placed near each gluteus maximus location and one each on the ventral aspect of pelvis superficially to the acetabulum.

Stepping over an object.

This will take place in the same manner as the normal walk (with tape on the floor to indicate the start and stop locations). In the center, between the tape markings, will be placed two shoe boxes that are stacked. When the subject is given the signal, they will walk toward the other piece of tape and lift their right leg up to step over the boxes. when they reach the other piece of tape, they will stop. This will be repeated and the left leg will be lifted first to step over the boxes. The third and fourth trials will allow the subject to step over the boxes with whichever foot they choose. The SEMG electrodes for this task will be identical to the locations indicated for stairs.

During each of the activities that allows the subject's choice of right vs. left, the side will be recorded and the trial for which it occurred.

There will be three separate study visits for each volunteer. During each visit they will perform all tasks described above. Each study visit will be separated by at least 2 but no more than 10 days.

Inclusion/Exclusion Criteria

The **inclusion** criteria is:

1) That a group of 20 volunteers will complete three trials each.
2) The patient is between 18 and 30 years of age.
3) Previously healthy as documented by a medical screening questionnaire (see attached) and normal vital signs.
    a. Blood pressure <140/90
    b. Resting heart rate between 50-100 beats/minute
    c. Oral temperature $\leq$ 37° C
4) The patient is considered reliable, willing, and able to give consent.

The **exclusion** criteria is:

1) Known medical condition affecting the cardiovascular, pulmonary, nervous, or musculoskeletal systems, or any other physical condition that would result in danger or discomfort to the subject when performing the tasks required by the study.
2) A mental condition that would interfere with the subject's cooperation with tasks required by the study or with the ability to follow-up reliably for the duration of the study.

Selection of Study Population

Patient Accrual

We intend to accrue at least 20 patients. We need at least 20 patients to finish all three testing visits; therefore if patients sign a consent form and then decide not to participate in the study we will find a new volunteer to take their place. Estimating a drop-out rate of 20%, we will presume that no more than 25 total patients should be needed in order to attain the 20 count for number of people that complete the study.

Estimated Duration of the Study

The proposed study will likely take 9 months for patient accrual and testing. All of the subjects we will enroll will be in excellent physical condition and have no health problems that could cause them to come back infrequently. Each of the testing sessions will be relatively short and it is not anticipated that this will cause unnecessary inconvenience to the volunteers.

Examinations, laboratory tests, procedures and follow-up visits

No laboratory tests will be involved with this study. A brief history and physical will be done for each consenting patient to confirm their good health. This history and physical will cover basics such as blood pressure and resting heart rate.

Drugs, Devices or Instruments to be Used

There are no drugs that will be involved with this research. Falling under the devices/instruments to be used category are the following: the Cognoscope, which is the instrument used for the near IR brain imaging and data collection, and also portable electromyographic equipment.

Data Analysis

The main goal of data analysis is to correlate data from the EMG sensors to the patterns in brain activity, and generate appropriate proactive triggers to the exoskeleton. The latter function will be fully researched once a clear correlation can be established between events generated by the muscles and patterns in the brain.

Two sets of data are generated – by the EMG sensors attached to various muscle groups and by the thought sensing device that is recording brain activity. EMG sensors are measuring voltages using sixteen different sensors at a rate of 20 samples per second or 20 Hertz. This is approximately a Megabyte of data every hour. Data thus generated is routinely logged to a database for archival purposes and to create a complete audit trail for offline analysis. No sensitive information is stored inside the database. The data is suitable to be exported to different team members without compromising the subject's privacy. Every new subject receives a unique ID that is used by the system to follow the subject.

One of the main difficulties in processing signals from EMG sensors is the noise that is associated. Generally, various filters or algorithms based on Independent Component Analysis are applied to refine the signal and suppress spurious artifacts. Correlation would be computed by either using one of the standard statistical packages such as MATLAB or by developing more refined methods based on modified nearest-neighbor algorithms.

In addition, the data capturing hardware would be integrated with a visualization subsystem. This would be an interactive, realtime correlation establishment and visualization software. It would also give the user the ability to tune different parameters for best performance. This visualization software would be built using graphical user

interfaces and lets the user focus on the signals that are being recorded. The user interface would offer two display modes: a normal view-mode and a quality view-mode. The quality view-mode displays the consecutive signals superimposed. This way it is easy to see if the signals change from one electrode to the other. Furthermore, in a separate window, the cross-correlation values would be displayed for all superimposed signals.
Checking the acquired signals during the acquisition is crucial for good signal quality.

Safety Management

The subjects will be informed of how the research is going to be conducted, what it is that we're monitoring, and why we want to find this information. Patients will immediately be informed if they are at risk (as determined by the principal investigator).

RISKS

Subjects

The risks involved in this study are minimal. The health of the patients will be previously determined to be excellent prior to any testing, therefore risk of a health problem is minimal. The activities that will be monitored are very simple motor tasks that should not be a problem for any volunteer to accomplish.

Investigators/Institutions

There are no known risks to the investigators.

Benefits

The goal of this research is to determine feasibility of using near IR for functional brain imaging and then implementing this technique in the future helmet portion of the Exoskeletons for Human Performance Augmentation. There are a number of other far-reaching applications not related to this particular project however. The platform technology developed by this research has the potential to expand into applications such as prosthetic control for paraplegics or even quadriplegics and even enhanced communication options for disabled.

Patient Compensation

Patients will be compensated for their time and travel at a rate of $20.00. At the completion of this study a check will be mailed to each participant that reflects the number of trials completed. If all three trials are completed then the subject will be sent a total of $60.00. If the subject chooses to withdraw from the study at some point or if they are removed from the study by the decision of the principal investigator, then they will be sent a check for the pro-rated amount of $20.00 per visit completed.

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Special Consent Issues

This is not an issue for the current project. Mentally handicapped and vulnerable subjects will not be included.

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